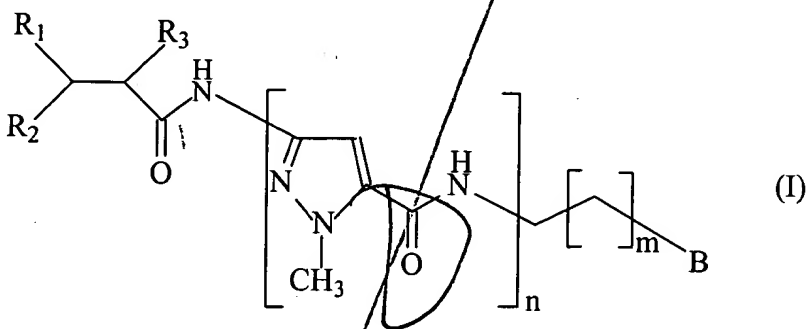


IN THE CLAIMS:

Please amend claims 1, 3, 5, 6, 9 and 11 as follows:

- B2 1. (Amended) A compound which is an acryloyl substituted distamycin derivative of formula



wherein:

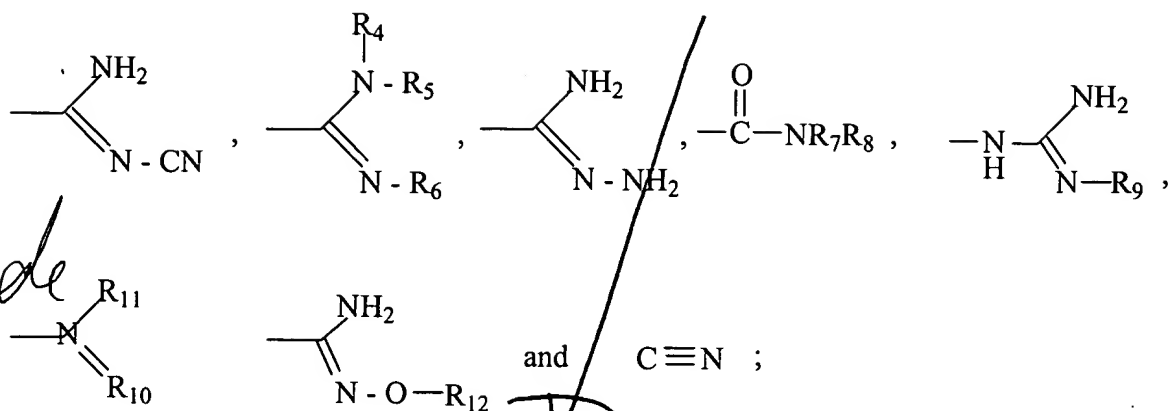
n is 2, 3 or 4;

m is 1 or 2;

R₁ and R₂, which are the same or different, are selected from hydrogen, halogen, and C₁-C₄ alkyl;

R₃ is hydrogen or halogen;

B is selected from



wherein R₄, R₅, R₆, R₇, R₈, R₁₀, R₁₁ and R₁₂ are, independently from each other, hydrogen or C₁-C₄ alkyl; and R₉ is hydrogen or hydroxy; or a pharmaceutically acceptable salt thereof; provided that

- a) if an R₄, R₅ or R₆ group is present, then at least one of R₄, R₅ and R₆ is alkyl; and
- b) at least one of the heterocyclic rings within the polyheterocyclic chain is other than pyrrole.

B3 3. (Twice Amended) A compound according to claim 1 wherein

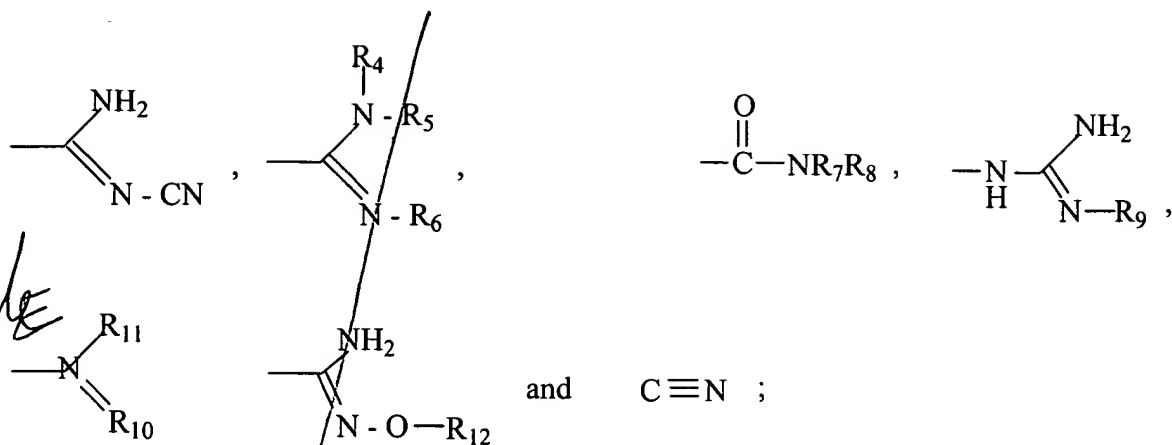
n is 3 or 4;

Sub D1 m is 1;

R₁ and R₂ are hydrogen;

R₃ is chlorine or bromine;

B is selected from



wherein R₄, R₅, R₆, R₇, R₈, R₁₀, R₁₁ and R₁₂ are, independently from each other, hydrogen or methyl; and R₉ is hydrogen.

- B4
C/MC1
5. (Amended) A compound selected from the group consisting of:
- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α-bromoacrylamido)-pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propioncyanamidine;
 - 3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α-bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N-methylamidine;
 - 3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α-chloroacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N-methylamidine;
 - 3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α-bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N,N'-dimethylamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N,N'-dimethylamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -chloroacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N,N'-dimethylamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N,N,N'-trimethylamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionamide;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N-methylamide;

2 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) ethylguanidine;

2 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -chloroacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) ethylguanidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propyl-N,N-dimethylamine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -chloroacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-O-methylamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -chloroacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-O-methylamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionitrile;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -chloroacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionitrile;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido)
pyrrole-2-carboxamido) propioncyanamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido)
pyrrole-2-carboxamido) propion-N-methylamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido)
pyrrole-2-carboxamido) propion-N,N'-dimethylamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido)
pyrrole-2-carboxamido) propion-N,N,N'-trimethylamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido))
pyrrole-2-carboxamido propionamide;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido)
pyrrole-2-carboxamido) propion-N-methylamide;

2 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido)
pyrrole-2-carboxamido) ethylguanidine;

2 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -chloroacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido)
pyrrole-2-carboxamido) ethylguanidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido)
pyrrole-2-carboxamido) propyl-N,N-dimethylamine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido)
pyrrole-2-carboxamido) propionamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -chloroacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido)
pyrrole-2-carboxamido) propionamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido)
pyrrole-2-carboxamido) propion-O-methylamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -chloroacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido)
pyrrole-2-carboxamido) propion-O-methylamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido)
imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido)
pyrrole-2-carboxamido) propionitrile;

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- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N-methylamidine;
- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(1-methyl-3-(α -chloroacrylamido) pyrazole-5-carboxamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N-methylamidine;
- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N,N'-dimethylamidine;
- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N,N,N'-trimethylamidine;
- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N-methylamide;
- 2 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) ethylguanidine;
- 2 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(1-methyl-3-(α -chloroacrylamido) pyrazole-5-carboxamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) ethylguanidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionitrile;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propioncyanamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N-methylamide;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N,N-dimethylamine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-O-methylamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionitrile;

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ant.
- 3 - (1-methyl-3-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrazole-5-carboxamido) propion-N-methylamidine;
- 3 - (1-methyl-3-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrazole-5-carboxamido) propion-N,N'-dimethylamidine;
- 2 - (1-methyl-3-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrazole-5-carboxamido) ethylguanidine;
- 3 - (1-methyl-3-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrazole-5-carboxamido) propionamidoxime;
- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) imidazole-2-carboxamido) propion-N-methylamidine;
- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) imidazole-2-carboxamido) propionamide;
- 2 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) imidazole-2-carboxamido) ethylguanidine;

- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) imidazole-2-carboxamido) propionamidoxime;
- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) imidazole-2-carboxamido)-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionamidoxime;
- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionitrile;
- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propioncyanamidine;
- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N-methylamidine;
- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(α -chloroacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N-methylamidine;
- 3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N,N'-dimethylamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N,N,N'-trimethylamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionamide;

2 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) ethylguanidine;

2 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(α -chloroacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) ethylguanidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(α -chloroacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-3-(α -bromoacrylamido) pyrazole-5-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionitrile;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propioncyanamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N-methylamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N,N'-dimethylamidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N,N,N'-trimethylamidine;

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Cont. 3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionamide;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N-methylamide;

2 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) ethylguanidine;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-N,N-dimethylamine.;

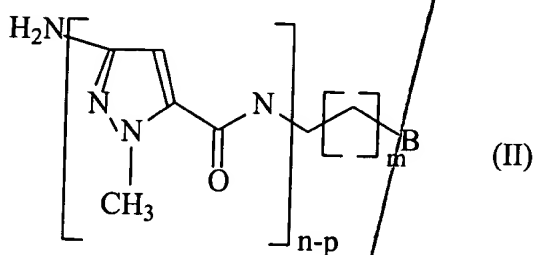
3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propion-O-methylamidoxime;

3 - (1-methyl-4-(1-methyl-4-(1-methyl-4-(α -bromoacrylamido) imidazole-2-carboxamido) pyrrole-2-carboxamido) pyrrole-2-carboxamido) propionitrile; and the pharmaceutically acceptable salts thereof.

6. (Amended) A process for preparing a compound as defined in claim 1, which process comprises:

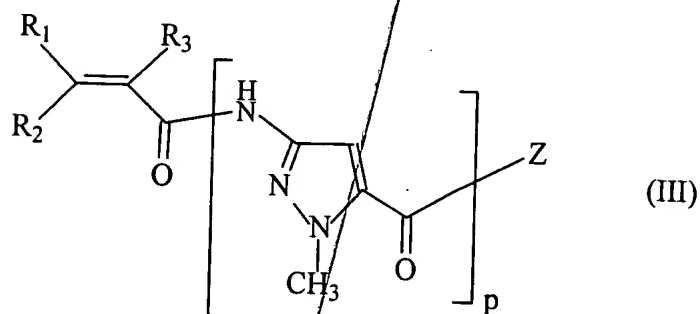
(a) reacting a compound of formula:



wherein n, m, and B are as defined in claim 1;

p is 0 or 1;

with a compound of formula:



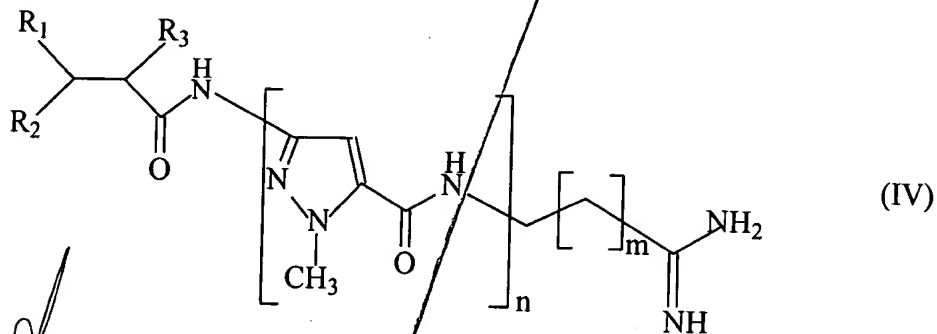
wherein R_1 , R_2 , and R_3 , are as defined in claim 1;

p is as defined above;

z is hydroxy or a leaving group;

or:

(b) when B is equal to $-C\equiv N$, reacting a compound of formula:



wherein n , m , R_1 , R_2 , and R_3 , are as defined above;

with succinic anhydride; and,

(c) if desired, converting a compound of formula (I) into a pharmaceutically acceptable salt thereof.

B3
Sub D3

9. (Amended) A compound as defined in claim 1 for use in a method of treatment of a human or animal body by therapy.

B3
Sub D3

11. (Amended) A method of manufacturing a medicament for use as an antitumor agent comprising utilizing a compound as defined in claim 1.